applicants' presumptively enabling specification does not, in fact, enable the claims. *In re Marzocchi*, 169 U.S.P.Q. 367 (CCPA 1971).

Here, the PTO appears to rely on discussions of gene therapy clinical effectiveness or scientific certainty rather than a standard for patent applications. (*See* page 3 of Paper No. 10, referring to "clinical efficacy," and the reference to definitive proof from the Scientific American review.) When the appropriate standard is applied here, applicants' claims are indeed enabled by the specification.

In discussing the appropriate standard of § 112, first paragraph, the M.P.E.P clearly states (at 2107.02):

> Thus, while an applicant may on occasion need to provide evidence to show that an invention will work as claimed, it is improper for Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness. *See In re Sichert*, 196 USPQ 209 (CCPA 1977); *In re Hartop*, 135 USPQ 419 (CCPA 1962); *In re Anthony*, 162 USPQ 594 (CCPA 1969); *In re Watson*, 186 USPQ 11 (CCPA 1975); *In re Krimmel*, 130 USPQ 215 (CCPA 1961); *Ex parte Jovanovics*, 217 USPQ 907 (Bd. Pat. App. & Inter. 1981). (emphasis in original)

The PTO's reasons for this rejection seem to fall squarely within the "degree of effectiveness" concern that the M.P.E.P. prohibits.

Furthermore, the Federal Circuit recently addressed the standard for § 112 and specifically distinguished the clinical data the FDA reviews. *In re Brana*, 34 U.S.P.Q.2d 1436, 1442 (Fed. Cir. 1995)("FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws."). The documents discussing clinical effectiveness and definitive proof do not seem to be relevant when the proper standard is applied.

Lastly, one skilled in the art was familiar with many different ways to use an expression system or cassette in a gene transfer technique. Examples from different methods involving, for example, plasmids, retroviruses, adeno-associated viruses, liposomes, and eletrotransfer techniques to name a few, could have been selected. One particular example can be found in the enclosed WO 99/01175 document (substitute Form 1449 provided). This document shows how one of skill in the art could have used techniques to improve gene delivery in a method that would seem very relevant to treating ALS. Plasmids, naked nucleic acids, or adenoviral vectors, for example, could be used to introduce the expression system of the claimed invention using the

electrotransfer technique. Since applicants have already demonstrated the use of the claimed invention, the selection of a desirable system for delivering the expression system would have been well within the skill of the ordinary artisan.

Applicants respectfully submit that there is no reason under the appropriate laws to require any additional showing that the claimed invention can be used. The Examples and specification demonstrate enabling uses. Applicants respectfully request withdrawal of this rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 26-51 stand rejected under 35 U.S.C. § 112, second paragraph, as the claims are allegedly indefinite. Applicants respectfully disagree.

At pages 4-5 of Paper No. 10, the PTO asserts that the term "expression system" is used in a manner inconsistent with the specification and is inconsistent with the use of the term "vector" in the claims. However, at page 7, lines 7-10, the specification states: "Advantageously, the expression system comprises a nucleic acid coding for a neurotrophic factor under the control of a transcriptional promoter (expression cassette)." As one of skill in the art would understand, an expression cassette may be contained in a vector, but an expression cassette need not be a vector. In claim 41, for example, the expression system is a vector that comprises a cassette for expressing two different neurotrophic factors. There is nothing unclear in the use of the claim language. Applicants cannot find anything inconsistent with the use of the term "expression system" or in the use of "vector" or "cassette." Clarification is respectfully requested.

The PTO also points to claim 29 as unclear in the use of the phrase "comprising two nucleic acids." As noted above from the quote from page 7 of the specification, the expression cassette comprises a nucleic acid coding for a neurotrophic factor and its associated promoter. If, as in claim 28, more than one coding region is included in this nucleic acid, then the nucleic acid can encode a different neurotrophic factor with respect to the first encoded neurotrophic factor. Claim 29, therefore, recites an expression system comprising one neurotrophic factor-encoding region and another, different neurotrophic factor-encoding region in the nucleic acid. Applicants submit this is understood by one of skill in the art.

The PTO points out that claim 49 is incomplete. Applicants have amended claim 49 to clearly indicate that "injectable" refers to an injectable form of the composition. Many places in the specification refer to an injectable form of a claimed composition, including page 32, lines 13-14. This aspect of the rejection has been overcome.

Applicants respectfully request withdrawal of this rejection.

Rejection under 35 U.S.C § 103

Claims 39-50 stand rejected under 35 U.S.C. § 103, as allegedly being unpatentable over Haase *et al.*

Applicants note that the Examiner referred to an English translation of the French priority document (page 6 of Paper No. 10). Applicants have enclosed an English translation of the French priority document. The translation, at pages 20-22, for example, details the type of compositions that are recited in claims 39-50. The remainder of the document also discloses the same type of expression system and neurotrophic factors disclosed in this application. Applicants submit that the French priority document adequately supports the claimed invention. The French priority document was filed prior to the publication of the Haase document. Thus, the Haase document is not proper "prior art" to this application. For at least this reason, applicants request withdrawal of this rejection.

## CONCLUSION

Applicants maintain that this application is in condition for allowance. If the Examiner believes that an interview with applicants' representative, either by telephone or in person, would further prosecution of this application, we would welcome the opportunity for such an interview.

Applicants have provided for an extension above. No additional extension of time fees, requests for extension of time, petitions, or additional claim fees are believed to be necessary to enter and consider this paper. If, however, any extensions of time are required or any fees are due in order to enter or consider this paper or enter or consider any paper accompanying this paper, including fees for net addition of claims, applicants hereby request any extensions or

petitions necessary and the Commissioner is hereby authorized to charge our Deposit Account # 50-1129 for any fees. If there is any variance between the fee submitted and any fee required, including the extension of time fee and fee for net addition of claims, the Commissioner is hereby authorized to charge or credit Deposit Account No. 50-1129.

Respectfully submitted,

WILEY REIN & FIELDING LLP

Dated: October 23, 2001

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APPENDIX 1: Marked-up version of Claim 49

49. (amended) The pharmaceutical composition according to claim 40, in an intravenously injectable form.

Previous claim 49. The pharmaceutical composition according to claim 40, in intravenously injectable.